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Autologous Cell Transplant Helpful in Ischemic **Heart** or Legs

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Nov. 18, 2002 — Autologous cell transplantion may benefit ischemic hearts and legs, according to three presentations on Nov. 18 at the American **Heart** Association's 75th Scientific Sessions held in Chicago, Illinois. Two studies focused on injecting autologous bone marrow cells or autologous skeletal myoblasts into the scarred area of an infarcted **heart**. In another study, injecting autologous bone marrow into ischemic limbs led to new vessel growth, reducing the need for amputation.

"Bone marrow not only can differentiate into **heart** cells, but also smooth muscle cells, connective **tissue** cells and other types of cells to reconstitute the entire structure of a **tissue**," presenter Manuel Galinanes, MD, from the University of Leicester in the U.K., says in a news release. "The benefit [of transplanting bone marrow into scar **tissue** of the **heart**] could be seen only six weeks **after** injection."

In 14 patients with low ejection fraction post-myocardial infarction (MI), autologous bone marrow from the sternum was injected into scarred myocardium during nonemergency coronary artery bypass surgery. **Heart** wall motion measured with echocardiography improved within weeks of treatment, and improvements persisted for at least 10 months **after** treatment.

The regional wall motion score decreased significantly, reflecting less movement abnormality, from a mean score of 2.41 at baseline to 2.16 six weeks **after** treatment and 2.09 ten months **after** treatment. The global wall motion score also decreased significantly from 1.96 before surgery to 1.64 at six weeks, and stabilized at 1.65 **after** 10 months.

Although it is still unproven that bone marrow creates a new cellular infrastructure in **heart** scar **tissue**, "that is the only possible explanation," Galinanes says. "The ability to confirm the presence of scar **tissue** with dobutamine stress echo before surgery, and then confirm it again during surgery, told us that the affected area was dysfunctional and the abnormality was irreversible. We wanted to make sure that we were injecting the marrow into **dead tissue** to help ensure that the injection would not pose any serious risk to the patient."

If additional studies confirm safety and efficacy, Galinanes says that this treatment would be a welcome addition to the post-MI arsenal, which also includes gene therapy, growth factor therapy, and laser treatments.

In a multicenter trial supervised by the U.S. Food and Drug Administration, investigators safely transplanted 16 patients with autologous skeletal myoblasts injected into hearts severely damaged by MI or **heart** failure. Baseline left-ventricular ejection fraction was less than 30%. Eleven patients were undergoing coronary artery bypass surgery and five were having implantation of a left ventricular assist device. Myoblasts extracted from thigh muscle were grown in large quantities in vitro using a controlled cell expansion manufacturing process, and were injected in doses ranging from 10 million to 300 million cells.

"We have been able to **regenerate dead heart** muscle, or scar **tissue**, in the area of **heart** attack without increasing risk of death. Our findings will allow us to move forward with testing if the procedure can improve the contractility of the **heart**," says lead author Nabil Dib, MD, from the Arizona **Heart** Institute in Phoenix. "We found that the transplanted myoblasts survived and thrived in patients. Areas damaged by **heart** attack and cardiovascular disease showed evidence of repair and viability."

Twelve weeks **after** transplant, mean ejection fraction rates improved from 22.7% to 35.8%, or a 58% increase. Echocardiogram, magnetic resonance imaging, and positron emission tomography showed evidence of regeneration in the area of the graft. There were no significant adverse events related to the cell transplant procedure at nine-month follow-up.

The third study showed that bone marrow cells implanted into ischemic legs in patients with peripheral arterial disease (PAD) formed new blood vessels, increased blood flow, and prevented amputation.

"This is the first multicenter and double-blind clinical study to prove the clinical efficacy of growing new blood vessels (angiogenesis) using bone marrow cell transplantation," says lead author Hiroya Masaki, MD, PhD, from Kansai Medical University in Osaka, Japan.

In this randomized trial, 45 patients with PAD received injections of autologous bone marrow mononuclear cells into the calf muscles. Compared with controls who received saline injections, patients who received bone marrow mononuclear cell transplants had a "striking" increase in new capillary formation and in newly visible collateral vessels.

Of 45 treated patients, 31 had an increase in ankle-brachial pressure index in the treated limbs, and 39 had decreased rest pain with improved treadmill endurance. Ischemic ulcers or gangrene healed in 21 of 28 treated limbs.

CD34-cells, which can develop into endothelial progenitor cells, expressed angiogenic growth factors including basic fibroblast growth factor, vascular endothelial growth factor, and angiopoietin-1. Although more research is needed to determine long-term efficacy and safety, "this new angiogenesis therapy using bone marrow cell transplantation may help many patients suffering with ischemic limbs," Masaki says.

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